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## REMARKS

Applicants herein canceled claim 1 without prejudice. The claim is canceled for the purpose of streamlining the Examiner's consideration of a Request for Interference filed concurrently herewith. Therefore, the claim is not canceled for any reason related to patentability and is canceled without prejudice or disclaimer. Applicants added claims 50-78. Therefore, claims 50-78 are presently before the Examiner for consideration. Entry of the amendment is respectfully requested. After entry of this amendment, claims 50-78 will be pending in the application.

Table A reflects the correlation of Applicants' claims vis-à-vis U.S. Patent No.'s 6,649,348. Applicants' claims 50-78 are identical to claims 1-29, respectively, of U.S. Patent No. 6,649,348 to Bass et al., issued November 18, 2003.

**Table A**

<b><u>Bass et al., U.S.P.No. 6,649,348</u></b>	<b><u>Applicants' Claims</u></b>
1	50
2	51
3	52
4	53
5	54
6	55
7	56
8	57
9	58
12	59
13	60
14	61
15	62
16	63
17	64
18	65
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24	68
25	69
26	70
27	71

Table B reflects disclosures in Applicants' specification which support newly added claims 73-78. As reflected in Table B, the newly added claims present no new matter.

**TABLE B**

<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
50. A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:	Page 2, lines 17-34; page 9, lines 7-22.
(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,	Page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.
(b) mounting said support in a chamber of a flow cell and subjecting said surface to one step of said synthesis and	Page 9, line 33 to page 10, line 4. Page 24, line 13 to page 29, line 13.
(c) mounting said support in a chamber of another flow cell and subjecting said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is mounted wherein said support is selected from the group consisting of a strip, a plate or a flat glass.	Page 9, line 27 to page 10, line 4. Page 46, line 4-30. Page 26, line 28-30. Page 27, lines 13-21. Page 11, lines 14-35.
51. A method according to claim 50 further comprising mounting said support after step (c) of said synthesis into a chamber of another flow cell and subjecting said surface to another step of said synthesis.	Page 9, line 33 to page 10, line 4; page 46, lines 6-31.
52. A method according to claim 50 wherein said synthesis comprises "n" number of steps including (b) and (C) and said method comprises independently mounting a support into a chamber of one of "n" number of flow cells and subjecting said surface to a different step of said synthesis in each of said flow cells.	Throughout and see USPNo. 5,143,854, which are incorporated by reference at page 16, line 26.
53. A method according to claim 50 wherein reagents for step (b) of said synthesis are in fluid communication with said flow cell of	Page 4, lines 3-23.

<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
step (b) and reagents for step (c) of said synthesis are in fluid communication with said flow cell of step (C) and wherein the fluid communication of the flow cell of step (b) is separate from the fluid communication of the flow cell of step (c).	
54. A method according to claim 50 wherein at least one of said steps of said synthesis comprises washing said surface.	Page 25, line 18, page 27, line 3, and page 38, lines 32-37.
55. A method according to claim 50 wherein said chemical compounds are polymers.	Page 6, line 15 to page 7, line 26.
56. A method according to claim 55 wherein said polymers are biopolymers.	Page 6, line 15 to page 7, line 26.
57. A method according to claim 50 wherein said flow cells comprise a holder for said support.	Page 46, line 34 to page 47, line 4.
58. A method according to claim 50 wherein said flow cells comprise at least one inlet and an outlet.	Page 26, lines 28 to 36, and page 27, lines 13-21.
59. A method according to claim 58 wherein a wash solution and a reagent for said synthesis are independently directed to said inlet.	Page 25, line 18, page 27, line 3, and page 38, lines 32-37. Fig. 6B.
60. A method for synthesizing an array of biopolymers on the surface of a support wherein said synthesis comprises a plurality of monomer additions, said method comprising:	Page 2, lines 17-34; page 9 7-22.
(a) depositing droplets of monomer addition reagents on a surface of said support,	Page 16, 29-30 for depositing droplets. See also, page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.
(b) placing said support into a chamber of a flow cell and subjecting said surface to a step of said synthesis that is subsequent to a monomer addition and	Page 9, line 33 to page 10, line 4. Page 24, line 13 to page 29, line 13.
(c) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis that is subsequent to step (b) wherein said steps are repeated until said array of biopolymers is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the	Page 9, line 27 to page 10, line 4. Page 46, line 4- 30.  Page 26, line 28-30.

<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
chamber in which the support is placed and wherein said flow cell of (b) is dedicated to said step (b) and said flow cell of (c) is dedicated to step (c).	Page 27, lines 13-21.
61. A method according to claim 62 wherein one of said steps (b) and (c) comprises a wash.	Page 25, line 18, page 27, line 3, and page 38, lines 32-37.
62. A method according to claim wherein said biopolymers are polynucleotides.	Page 6, line 23, lines 32-38.
63. A method according to claim wherein step (b) comprises subjecting said surface to an oxidizing agent.	Page 38, lines 2-31.
64. A method according to claim wherein step (c) comprises subjecting said surface to an agent for removing a protecting group.	Page 38, lines 2-31.
65. A method according to claim wherein said flow cells comprise at least one inlet and an outlet and a holder for said support.	Page 46, line 34 to page 47, line 4. Page 26, lines 28 to 36, and page 27, lines 13-21.
66. A method according to claim 67 wherein a wash solution and a reagent for said synthesis are independently directed to said inlet.	See Figure 6A, Page 25, lines 5-22.
67. A method according to claim wherein said biopolymers are peptides.	Page 6, line 21.
68. A method according to claim wherein said biopolymers are synthesized on said surface in multiple arrays and said support is subsequently diced into individual arrays of biopolymers on a support.	Page 49, lines 13-15, page 49, line 37 to page 50, line 23.
69. A method according to claim wherein reagents for said first step of said synthesis are in separate fluid communication with said first flow cell and reagents for said second step of said synthesis are in separate fluid communication with said second flow cell.	Figure 3A & 3B, of 14 line 63.
70. A method according to claim further comprising exposing the array to a sample and reading the array.	See page 53, line 30 to page 55, line 11. See page 54, lines 35 to page 55, line 4 for detection.
71. A method according to claim 71 comprising forwarding data comprising a result obtained from a reading of the array.	See page 53, line 30 to page 55, line 11. See page 54, lines 35 to page 55, line 4 for detection.
72. A method according to claim 71 comprising receiving data comprising a result of an interrogation obtained by the reading of	See page 53, line 30 to page 55, line 11. See page 54, lines 35 to page 55, line 4 for detection.

<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
the array.	
73. A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:	Page 2, lines 17-34; page 9, lines 7-22.
(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,	Page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.
(b) placing said support in a chamber and subjecting said surface to one step of said synthesis and	Page 9, line 33 to page 10, line 4.  Page 24, line 13 to page 29, line 13.
(c) placing said support in another reaction chamber and subjected said surface to another step of said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said reaction chambers comprises an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed wherein said support is selected from the group consisting of a strip, a plate or a flat glass.	Page 9, line 27 to page 10, line 4.  Page 46, line 4- 30.  Page 26, line 28-30.  Page 27, lines 13-21.  Page 11, lines 14-35.
74. A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:	Page 2, lines 17-34; page 9, lines 7-22.
(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,	Page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.
(b) mounting said support in a chamber of a flow cell and subjecting said surface to one step of said synthesis and	Page 9, line 33 to page 10, line 4.  Page 24, line 13 to page 29, line 13.
(c) mounting said support in a chamber of another flow cell and subjecting said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is mounted wherein said support is selected from the group consisting of a strip, a plate or a flat glass.	Page 9, line 27 to page 10, line 4.  Page 46, line 4- 30.  Page 26, line 28-30.  Page 27, lines 13-21.  Page 11, lines 14-35.
75. A method for synthesizing an array of	Page 2, lines 17-34; page 9, lines 7-22.

<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
chemical compounds on the surface of a support, said method comprising:	
(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,	Page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.
(b) mounting said support in a chamber of a flow cell and subjecting said surface to one step of said synthesis and	Page 9, line 33 to page 10, line 4. Page 24, line 13 to page 29, line 13.
(c) mounting said support in a chamber of another flow cell and subjecting said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is mounted wherein said support is selected from the group consisting of a strip, a plate or a flat glass.	Page 9, line 27 to page 10, line 4. Page 46, line 4-30. Page 26, line 28-30. Page 27, lines 13-21. Page 11, lines 14-35.
76. The method of claim 73 further comprising modifying said chambers to perform multiple independent steps of said synthesis.	Page 46, lines 4-32.
77. The method of claim 74 further comprising modifying said chambers to perform multiple independent steps of said synthesis.	Page 46, lines 4-32.
78. The method of claim 75 further comprising modifying said chambers to perform multiple independent steps of said synthesis.	Page 46, lines 4-32.

Entry of the foregoing is respectfully requested.

Respectfully submitted,  
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Date: 3-26-04

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File No. 1084D

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: )  
MARTIN GOLDBERG et al ) Examiner: TBD  
Serial No. 10/722,032 ) Art Unit: 1646  
Filed: November 25, 2003 ) Request for Declaration of Interference  
For: SUBSTRATE PREPARATION PROCESS ) with a Patent under 37 CFR §1.607 -  
  ) Expedited Handling  
  )  
  )

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COMMISSIONER OF PATENTS  
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Sir:

## REMARKS

In accordance with 37 C.F.R. §1.607, Applicants hereby request an interference with United States Patent No. 6,649,348, which issued to Bass et al. on November 18, 2003. To facilitate consideration of this request, Applicants attach a proposed PTO-850 “Interference Initial Memorandum” outlining the requested interference.

Applicants herein comply with the provisions of 37 C.F.R. §1.607, which requires the following:

- (1) Identify the patent;
- (2) Present a proposed count;
- (3) Identify at least one claim in the patent corresponding to the proposed count;
- (4) Present at least one claim corresponding to the proposed count or identify at least one claim already pending in its application that corresponds to the proposed count, and, if any claim of the patent or application identified as corresponding to the proposed count does not correspond exactly to the proposed count, explain why each such claim corresponds to the proposed count; and
- (5) Apply the terms of any application claim,
  - (i) Identified as corresponding to the count, and
  - (ii) Not previously in the application to the disclosure of the application.

- (6) Explain how the requirements of 35 U.S.C. § 135(b) are met, if the application claim identified as corresponding to the proposed count was not present in the application until more than one year after the issue date of the patent.

**37 C.F.R. §1.607(a)(1) - Identification of Involved Patent**

In accordance with 37 C.F.R. §1.607(a)(1), Applicants identify U.S. Patent No. 6,649,348 to Bass et al. ("the '348 patent").

**37 C.F.R. §1.607(a)(2) - Proposed Count**

In accordance with 37 C.F.R. §1.607(a)(2), Applicants propose a count defined as follows:

Claim 1 of the '348 patent

or

Applicants' Claim 73

Claim 1 of the '348 patent reads as follows:

A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:

- (a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,
- (b) mounting said support in a chamber of a flow cell and subjecting said surface to one step of said synthesis and
- (c) mounting said support in a chamber of another flow cell and subjecting said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells

comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is mounted wherein said support is selected from the group consisting of a strip, a plate or a flat glass.

Applicants' claim 73 reads as follow:

A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:

(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,

(b) placing said support in a reaction chamber and subjecting said surface to one step of said synthesis and

(c) placing said support in another reaction chamber and subjecting said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said reaction chambers comprises an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed wherein said support is selected from the group consisting of a strip, a plate or a flat glass.

#### **37 C.F.R. §1.607(a)(3) - Patent Claims Corresponding to the Proposed Count**

In accordance with 37 C.F.R. §1.607(a)(3), Applicants identify claims 1-29 of the '348 patent as corresponding to the proposed count. Claim 1 is expressly recited in the definition of the proposed count and claims 2-29 define the same patentable invention as the proposed count, as explained below.

#### **37 C.F.R. §1.607(a)(4) - Application Claims Corresponding to the Proposed Count**

In accordance with 37 C.F.R. §1.607(a)(4), Applicants identify Applicants' claims 50-78 as corresponding to the proposed count. Applicants' claim 73 is expressly recited in the

definition of the proposed count and Applicants' claims 50-78 define the same patentable invention as the proposed count, as explained below.

### **37 C.F.R. § 1.601(n) - Claims Defining The Same Patentable Invention**

37 C.F.R. § 1.601(n) provides, in part, as follows:

Invention "A" is the *same patentable invention* as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

In the context of this request for interference, a claim (*i.e.*, "Invention A") is directed to the same patentable invention as a proposed count (*i.e.*, "Invention B") when the claim is the same or is obvious in view of the proposed count, assuming the proposed count is prior art with respect to the claim. Below, Applicants explain why the identified patent and application claims define the same patentable invention as the proposed count and, therefore, should be designated as corresponding to the proposed count.

#### **Claims 2-29 of the '348 Patent**

Claims 2-29 of the '348 patent define the same patentable invention as the proposed count and, therefore, should be designated as corresponding to the proposed count for at least the following reasons:

1. **Claim 2.** Claim 2 is expressly recited in the definition of the proposed count.

Therefore, claim 2 defines the same patentable invention as the proposed count.

2. **Claim 3.** Claim 3 depends from claim 1 and further recites “n” number of steps.

This limitation is incorporated within the definition of the proposed count and therefore defines the same patentable invention as the proposed count.

3. **Claim 4.** Claim 4 depends from claim 1 and is further limited to having the reagents of each step in fluid communication with the flow cell of that step. It would have been obvious to one of ordinary skill in the art to fluidly connect the reagents with the flow cell of each step in view of the method defined by the proposed count. The proposed count recites a method for synthesizing an array. It was well known in the art that a flow cell would be used and that the flow cell would be fluidly connected to the reagents used in the flow cell. See for example U.S. Patent No. 5,424,186 ('186) issued June 1995, Figs. 22A and B and accompanying text at col. 32, lines 22-67. See also, U.S. Patent No. 5,959,098 ('098) issued September 28, 1999, Fig. 3A and 3B at col. 14, line 57 to col. 15, line 12. Both '186 and '098 are references under 35 USC §102(b). Other passages of both '186 and '098 are also pertinent. ('186 is incorporated by reference in '098 at col. 14, lines 53 to 56). Other general peptide and nucleic acid synthesis references that show the above limits are found at col. 22, lines 32 to 49 of '098 and col. 58, line 41 to col. 59, line 4 of '186 and serve to outline the general process steps of these dependent claims.

4. **Claim 5.** Claim 5 depends from claim 1 and is further limited to having a wash step. It would have been obvious to one of ordinary skill in the art to wash the synthesis surface. For example, see '186 generally, but specifically at col. 2, line 42 and various examples from col. 23 to 34. See also '098 at col. 15, line 8, and col. 16, line 3, as examples.

5. **Claim 6.** Claim 6 depends from claim 1 and further limits the chemical compounds to polymers. It would have been obvious to one of ordinary skill in the art to synthesize polymers as generally shown in '186, and specifically at col. 7, lines 34 to 63. See also '098 at col. 4, lines 47 to 64. There are multiple other locations in both documents, but the above passages suffice.

6. **Claim 7.** Claim 7 depends from claim 6 and further limits the polymers to biopolymers. It would have been obvious to one of ordinary skill in the art to synthesize polymers as generally shown in '186, and specifically at col. 7, lines 34 to 63. See also '098 at col. 4, lines 47 to 64. There are multiple other locations in both documents, but the above passages suffice.

7. **Claim 8.** Claim 8 depends from claim 1 and further limits the flow cells to include a holder. It would have been obvious to one of ordinary skill in the art to include a holder as generally shown in '098 in Fig. 6B and the accompanying text at col. 27, lines 20 to 47.

8. **Claim 9.** Claim 9 depends from claim 1 and further limits the flow cells to contain at least one inlet and at least one outlet. It would have been obvious to one of ordinary skill in the art to have an inlet and an outlet as shown in '186 at Figs. 22A and B and accompanying text at col. 32, lines 22-67 and Figs. 3A and 3B at col. 14, line 57 to col. 15, line 12. Figs. 6A and 6B and accompanying text at col. 26, line 66 to col. 27, line 37, at least. Other passages of both '186 and '098 are also pertinent.

9. **Claim 10.** Claim 10 is dependent on claim 9 and further limits the method to determining a condition of the fluid exiting the outlet and directing the fluid to the inlet or a waste container based on the determination. It would have been obvious to one of ordinary skill in the art to analyze the fluid and recycle or discard the fluid based on general process considerations as shown in any of a number of references, such as:

- 1) Guo, Zhiqiang; Pfundheller, Henrik M.; Sanghvi, Yogesh S. *Organic Process Research & Development* (1998), 2(6), 415-417. (See page 416, right col.).
- 2) Carlo L. Scremen, Liang Zhou, Kasturi Srinivasachar, Serge L. Beaucage; *J. Org. Chem.* 1994; 59:1963-1966. (See page 1964, right col.).
- 3) W. K-D. Brill; *Tetrahedron* 1994; 35:3041-3044. (See page 3043, third full paragraph).
- 4) Gough, G. R.; Brunden, M. J.; Gilham, P. T. *Tetrahedron Letters* (1981), 22(42), 4177-80.
- 5) Sanghvi, Yogesh S.; Ravikumar, V. T.; Scozzari, Anthony N.; Cole, Douglas L. Development Chemistry and Pharmaceutics, Isis Pharmaceuticals, Inc., Carlsbad, CA, USA. *Pure and Applied Chemistry* (2001), 73(1), 175-180.
- 6) Smrt, Jiri; Arnold, Lubos; Svoboda, Jan; Hak, Roman; Rosenberg, Ivan. *Inst. Org. Chem. Biochem., Acad. Sci. Czech Republic, Prague, Czech Rep.* Collection of *Czechoslovak Chemical Communications* (1993), 58(7), 1692-8. (see page 1697).

10. **Claim 11.** Claim 11 is dependent on claim 9 and further limits the method to subjecting the fluid exiting the outlet to purification and determining a condition of the fluid to thereby direct the fluid to the inlet or a waste container. It would have been obvious to one of

ordinary skill in the art to perform this process as shown in any of a number of references above as applied to claim 10.

11. **Claim 12.** Claim 12 depends from claim 9 and further states that the wash and reagent solutions are independently directed to the inlet. It would have been obvious to one of ordinary skill in the art to have the wash and reagent solutions are independently directed to the inlet as shown in '186 at Figs. 22A and B and '098 at Fig 3A and B and the accompanying text at col. 14, line 64.

12. **Claim 13.** Claim 13 is an independent claim which is different from claim 1 in that it is broader in not referring to a substrate shape or a mounting. It is narrower in the description of how reagents are placed on the surface of the support (depositing droplets of monomer addition reagents) and that the compound is a biopolymer. It would have been obvious to one of ordinary skill in the art to show how reagents are placed on the surface of the support as shown in '098 at col. 9, lines 60 to 67. PCT Application 93/09668 ('668) shows at Figs. 11 and 12 and pages 25 to 29 the deposition of droplets of monomer addition reagents of a surface of a support to form an array.

13. **Claim 14.** Claim 14 depends from claim 13 and is further limited to having a wash step. It would have been obvious to one of ordinary skill in the art to wash the surface of the synthesis surface. For example, see '186 generally, but specifically at col. 2, line 42 and various examples from col. 23 to 34. See also '098 at col. 15, line 8, and col. 16, line 3 as examples.

14. **Claim 15.** Claim 15 depends from claim 13 and further limits the biopolymers to polynucleotides. It would have been obvious to one of ordinary skill in the art to synthesize polynucleotides as generally shown in '186, and specifically at col. 7, lines 34 to 63. See also '098 at col. 4, lines 47 to 64. There are multiple other locations in both documents, but the above passages suffice.

15. **Claim 16.** Claim 16 depends from claim 13 and further limits the claim to subjecting the surface to an oxidizing agent. It would have been obvious to one of ordinary skill in the art to subject the surface to an oxidizing agent as generally shown in '186, and specifically at col. 66, line 36 and 43, col. 67, line 2, etc. See also '098 at col. 33, lines 13-33. See also '668 at page 41, lines 1 to 5 and the references generally describing the process therein. There are multiple other locations in both documents, but the above passages suffice.

16. **Claim 17.** Claim 17 depends from claim 13 and further limits the claim to subjecting the surface to an agent for removing a protecting group. It would have been obvious to one of ordinary skill in the art to subject the surface to an oxidizing agent as generally shown in '186, and specifically at col. 66, lines 24 to col. 67, line 2, etc. See also '098 at col. 33, lines 13-33. See also '668 at page 41, lines 1 to 5 and the references generally describing the process therein. There are multiple other locations in both documents, but the above passages suffice.

17. **Claim 18.** Claim 18 depends from claim 13 and further limits the flow cells to contain at least one inlet and at least one outlet. It would have been obvious to one of ordinary skill in the art to have an inlet and an outlet as shown in '186 at Figs. 22A and B and

accompanying text at col. 32, lines 22-67 and Figs. 3A and 3B at col. 14, line 57 to col. 15, line 12. See also '098 at Figs. 6A and 6B and accompanying text at col. 26, line 66 to col. 27, line 37, at least. Other passages of both '186 and '098 are also pertinent.

18. **Claim 19.** Claim 19 is dependent on claim 18 and further limits the method to subjecting the fluid exiting the outlet to purification and determining a condition of the fluid to thereby direct the fluid to the inlet or a waste container. It would have been obvious to one of ordinary skill in the art to perform this process as shown in any of a number of references discussed above in relation to claim 10.

19. **Claim 20.** Claim 20 depends from claim 13 and further states that the wash and reagent solutions are independently directed to the inlet. It would have been obvious to one of ordinary skill in the art to have the wash and reagent solutions are independently directed to the inlet as shown '098 at Fig 3A and B and the accompanying text at col. 14, line 64.

20. **Claim 21.** Claim 21 is dependent on claim 13 and further limits the method to determining a condition of the fluid exiting the outlet and directing the fluid to the inlet or a waste container based on the determination. It would have been obvious to one of ordinary skill in the art to analyze the fluid and recycle or discard the fluid based on general process considerations as shown in any of a number of references. For example, see the references cited above with respect to claim 10.

21. **Claim 22.** Claim 22 depends from claim 21 and further states that the fluid is an organic solvent. It would have been obvious to one of ordinary skill in the art to have fluid be an organic solvent as shown in '186 generally and in the general amino acid and nucleic acid

synthesis references, more specifically at Fig. Table 9 (use of Dioxane). See also '098 at col. 14, line 13, col. 28, lines 10 to 31 and other sections in the patent. Other general peptide and nucleic acid synthesis references are found at col. 22, lines 32 to 49 of '098 and col. 58, line 41 to col. 59, line 4 of '186 and serve to outline the general process steps of these dependent claims.

22. **Claim 23.** Claim 23 depends from claim 13 and further limits the biopolymers to peptides. It would have been obvious to one of ordinary skill in the art to synthesize peptides as generally shown in '186, and specifically at col. 7, lines 34 to 63. See also '098 at col. 4, lines 47 to 64. There are multiple other locations in both documents, but the above passages suffice.

23. **Claim 24.** Claim 24 depends from claim 13 and further limits the method to synthesizing biopolymers on the surface and dicing the support into individual arrays. It would have been obvious to one of ordinary skill in the art to synthesize biopolymers as shown above. Regarding the dicing step it would have been obvious to dice a support as shown in '098 at col. 28, line 55 to col. 47 and the references cited therein, such as PCT application No. 95/33846.

24. **Claim 25.** Claim 25 depends from claim 13 and limited by requiring that the reagents from the first step are in separate fluid communication with the first flow cell and reagents for the record step are in separate fluid communication with the second flow cell. It would have been obvious to one of ordinary skill in the art to use separate fluid communication to separate flow cells as shown in '186 in Figures 22A and B and '098 in Figures 3A and B and 6A.

25. **Claim 26.** Claim 26 depends from claim 13 and further limits the method to exposing the array to a sample and reading the array. It would have been obvious to one of ordinary skill in the art to exposing a sample to an array as generally shown in '186, and specifically at Figs. 39 A-C, col. 3, lines1 to 24, and the example at col. 66, line 50 to col. 68, line 19. See also '098 at col. 31, line 17 to col. 32, line 5. There are multiple other locations in both documents, but the above passages suffice.

26. **Claim 27.** Claim 27 depends from claim 13 and further limits the method to forwarding data comprising a result obtained from a reading of the array. It would have been obvious to one of ordinary skill in the art to forward of result of reading the array as generally shown in U.S. Patent No. 6,420,108 at Fig. 3 which shows that data is obtained in step 120, formed into an image file in step 124, forwarded to a computer in step 126 for analysis and then forwarded to step 128 for mutation analysis. See also col. 4, lines 39 to 45. See also EP 1 024 200 at paragraph 0072 where it states "Fig. 1B depicts the interconnection of computer system 10 to remote computers 48, 50, and 52. Fig. 1B depicts a network 54 interconnecting remote servers 48, 50, and 52. Network interface 46 provides the connection from client computer system 10 to network 54. Network 54 can be, e.g., the Internet. Protocols for exchanging data via the Internet and other networks are well known. Information identifying the polymorphisms described herein can be transmitted across network 54 embedded in signals capable of traversing the physical media employed by network 54."

27. **Claim 28.** Claim 28 depends from claim 27 and further limits the method to forwarding data to a remote location. It would have been obvious to one of ordinary skill in the art to forward of result of reading the array as generally shown in U.S. Patent No.

6,420,108 at Fig. 3 which shows that data is obtained in step 120, formed into an image file in step 124, forwarded to a computer in step 126 for analysis and then forwarded to step 128 for mutation analysis. See also col. 4, lines 39 to 45. See also EP 1 024 200 at paragraph 0072 as noted above for claim 27.

28. **Claim 29.** Claim 29 depends from claim 26 and further limits the method to receiving data comprising a result of an interrogation obtained by the reading of the array. It would have been obvious to one of ordinary skill in the art to forward of result of reading the array as generally shown in U.S. Patent No. 6,420,108 at Fig. 3 which shows that data is obtained in step 120, formed into an image file in step 124, forwarded to a computer in step 126 for analysis and then forwarded to step 128 for mutation analysis. See also col. 4, lines 39 to 45. See also EP 1 024 200 at paragraph 0072 as noted above in claim 27.

**37 C.F.R. §1.607(a)(6) - Applicants Have Satisfied The Requirements of 35 U.S.C. § 135(b)**

In accordance with 37 C.F.R. §1.607(a)(6), Applicants have complied with the requirements of 35 U.S.C. §§135(b)(1) and (2).

With regard to 35 U.S.C. § 135(b)(1), the '348 patent issued on November 18, 2003 and, therefore, Applicants present claims 50-78 with this Request in an amendment filed concurrently herewith which is less than one year after the issue date of the '348 patent. Accordingly, Applicants have satisfied the requirements of 35 U.S.C. § 135(b)(1).

With regard to 35 U.S.C. § 135(b)(2), the application from which the '348 patent issued (USSN 09/896,572) was published on January 2, 2003, *i.e.*, more than one year prior to the date on which Applicants presented claims 50-78. See U.S. Published Application No. 2003/0003222. However, the published independent claims do not have the same claim scope as those that were issued on November 18, 2003. For example, the published claims have new limitations that were required under 35 USC §§112, 102, and 103 as shown below.

The text of the independent, and some dependent, claims below is highlighted to show amendments made for purposes related to 35 USC § 112 and 103. The underlined text was added to address § 112 rejections and the bolded text addresses the prior art.

<u>'348 issued patent claims</u>	<u>Amendments to Secure Allowance</u>
1. A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising: <u>(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,</u>	Amended to comply with 35 U.S.C. § 112 in Amendment dated 12/4/2002 (Exhibit 1)
<u>(b) mounting said support in a chamber of a flow cell and subjecting said surface to one step of said synthesis and</u>	Added to overcome Kedar ref. in the Examiner's Amendment dated 3/07/2003 (Exhibit 2)
<u>(c) mounting said support in a chamber of another flow cell and subjecting said surface to another step of said synthesis</u>	Added to overcome Kedar ref. in the Examiner's Amendment dated 3/07/2003 (Exhibit 2)
<u>wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is mounted</u>	Amended to comply with 35 USC §§112 and 103, the text in bold shows amendments to overcome Ellman reference in Amendment dated 12/4/2002 (Exhibit 1)
<u>wherein said support is selected from the group consisting of a strip, a plate or a flat glass</u>	Added to overcome Kedar ref. in the Examiner's amendment dated 3/07/2003 (Exhibit 2)

<u>'348 issued patent claims</u>	<u>Amendments to Secure Allowance</u>
2. A method according to claim 1 further comprising mounting said support after step (c) of said synthesis into a chamber of another flow cell and subjecting said surface to another step of said synthesis.	Added to overcome Kedar ref. in the Examiner's amendment dated 3/07/2003 (Exhibit 2)
3. A method according to claim 1 wherein said synthesis comprises "n" number of steps <u>including (b) and (c)</u> and said method comprises independently mounting a support into a chamber of one of "n" number of flow cells and subjecting said surface to a different step of said synthesis in each of said flow cells.	Amended to comply with 35 U.S.C. §112 in Amendment dated 12/4/2002 (Exhibit 1)
4. A method according to claim 1 wherein reagents for step (b) of said synthesis are in fluid communication with said flow cell of step (b) and reagents for step (c) of said synthesis are in fluid communication with said flow cell of step (c) <u>and wherein the fluid communication of the flow cell of step (b) is separate from the fluid communication of the flow cell of step (c).</u>	Amended to comply with 35 USC §112 in Amendment dated 12/4/2002 (Exhibit 1)
13. A method for synthesizing an array of biopolymers on the surface of a support wherein said synthesis comprises a plurality of monomer additions, said method comprising:  (a) depositing droplets of monomer addition reagents on a surface of said support  (b) placing said support into a chamber of a flow cell and subjecting said surface to a step of said synthesis that is subsequent to a monomer addition and	Amended in Amendment dated 12/4/2002 (Exhibit 1)

<u>'348 issued patent claims</u>	<u>Amendments to Secure Allowance</u>
<p>(c) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis that is subsequent to step (b) <u>wherein said steps are repeated until said array of biopolymers is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed and wherein said flow cell of (b) is dedicated to said step (b) and said flow cell of (c) is dedicated to step (c).</u></p>	<p>Amended to comply with 35 USC §§112 and 103, the text in bold shows amendments to overcome Ellman reference in Amendment dated 12/4/2002 (Exhibit 1)</p>

The above chart shows that the claims were substantially amended during prosecution for reasons related to 35 U.S.C. §§102, 103 and 112. Claims 3,4, 13-29, 22, 26-29, 27 and 29 were rejected for indefiniteness under 35 USC §112. The examiner made various statements regarding claim clarity and Bass et al. revised their claims to obtain allowable subject matter in view of those rejections.

Also, substantial amendments were made to overcome at least two references. Bass made several statements that the amendments in the independent claims were made in order to overcome the Ellman and Kedar references. See page 8, last paragraph in the 102 discussion for the statement that justifies the inclusion of the language above to claims 1 and 13 regarding flow cell structure:

Without in any way acquiescing in the argument of the Examiner with respect to the relevance of Ellman's disclosure of pins and containers fro reagents, Applicant submits that the claims as amended obviate this ground of rejection. The claims now recite that the flow cells comprise a housing with a chamber in which the support is placed.

These limitations were not present in the originally published claim set and were required to define over the art.

Also, Bass amended claim 13 to include a limitation that was not present in the original claim set which substantially narrows the scope of the claim. It is shown in the chart above and is as follows: “depositing droplets of monomer addition reagents on a surface of said support”. This limit renders the claim substantially different from published claim 13. Other limitations that were required by the Examiner to overcome prior art references are not in this claim as it seems that this limitation was introduced in place of those other limitations. For example, claim 1 has the limitation “wherein said support is selected from the group consisting of a strip, a plate or a flat glass”. This limitation was added to overcome Kedar ref. in the Examiner’s amendment dated 3/07/2003, but is not present in claim 13. This would imply that the “depositing droplet” limit was made in place of the amendment to overcome Kedar. Otherwise, the claim would be invalid as shown below. Additionally, “placing” still remains in the claim and was not replaced by “mounting”. This limit was required to overcome the teaching of Kedar as shown below in the Examiner’s statement.

Additionally, see the language in the Examiner’s interview and her Examiner’s amendment and reasons for allowance which state:

Mr. Leitereg contacted the examiner to discuss the amendments which were suggested by the examiner to Mr. Stewart on 29 January i.e. in claim 1, limiting the support to a strip, a plate of flat glass and replacing “placing, into” of steps b and c with “mounting in”. Mr. Leitereg stated that he had reviewed the Kedar reference and agreed that the Kedar method is drawn to synthesis on beads. The examiner further explained reasons for amending claim 1 to limit the support and the method of “placing”, those reasons being that both amendments are required to overcome the teaching of Kedar

wherein beads are placed into a chamber of a flow cell and without both amendments, the instant claims would be obvious over Kedar.

Mr. Leitereg suggested that claim 1 be amended to limit the support to a “flat” support instead of the “strip, Plate, or flat glass” as suggested by the examiner. The examiner stated that “flat” support is a much broader description of the support than that provided by the specification. The examiner explained that pages 6-7 of the specification recites a long list of possible supports, but the list does not teach or describe the genus encompassed by the phrase “flat support”. Instead, the list on pages 6-7 includes numerous support compositions and shapes but the only supports described in the specification which are not encompassed by the Kedar beads are the strip, plate and flat glass.

Mr. Leitereg and the examiner discussed the method steps which recite “placing said support into a chamber of the flow cell”. The examiner stated that “placing” is a very broad term encompassing non-specific placement of the support into a chamber and Kedar places the beads supports into chambers of flow cell (e.g. Column 62, lines 17-65). The examiner stated that the instant invention, as described in the specification, differs from the Kedar reference by “mounting the support in the chamber of the flow cell” (page 14). Mr. Leitereg suggested that the claim be amended to limit the “placing” by language describing insertion of the support into the chamber through an opening independent of the inlet and outlet ports, the passengers cited not described such an opening. The examiner pointed to pages 16 and 22 for a teaching of a means (i.e. transfer robot) for transferring the supports from one flow cell chamber to another. The examiner suggested that claim 1 be amended to either replace “placing into” with “mounting in” or to insert limitations of a placing the support using a transfer robot.

The Examiner stated in the reasons for allowance that the new amendments to the claims overcame Kedar:

Kedar (U.S. Patent No. 6,165,778 issued 26 December 2000) teaches a method of synthesis comprising moving a plurality of beads in suspension into and out of reaction chamber for sequential addition of monomers onto the beads to thereby synthesize polymers on the beads (Abstract). Kedar specifically teaches the method is drawn to synthesis on beads in suspension. However, Kedar does not teach or suggest the suspended supports are comprised of a strip, plate or flat glass nor does Kedar teach that the suspended supports are mounted in the reaction chamber as instantly claimed. As such, the prior art of record does not teach or suggest the instantly claimed invention

These amendments resulted from the Response dated 12/4/2002 and a subsequent Examiner's amendment dated 3/07/2003. Accordingly, the published application claims do not

define the same or substantially the same invention as Applicants' claims 50-78 and, therefore, the published application claims do not raise a bar against Applicants' claims under 35 U.S.C. §135(b) (2).

In view of the above, Applicants have complied with the requirements of 35 U.S.C. §135(b).

**Benefit of Earlier Filed Application**

For the purpose of the requested interference, Applicants are entitled to the benefit of the April 17, 1996, filing date of USSN 08/634,053, now U.S. Patent No. 5,959,098, which constitutes a constructive reduction to practice of an embodiment within the scope of the proposed count. The undersigned hereby certifies that the specification of the instant application is substantially identical to the specification of the '053 application. The specification of the '053 application constitutes a constructive reduction to practice of subject matter within the scope of the proposed count, as reflected in the Table below:

<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
50. A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:  (a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,  (b) mounting said support in a chamber of a flow cell and subjecting said surface to one step of said synthesis and	Page 2, lines 17-34; page 9, lines 7-22.  Page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.  Page 9, line 33 to page 10, line 4.  Page 24, line 13 to page 29, line 13.

(c) mounting said support in a chamber of another flow cell and subjecting said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is mounted wherein said support is selected from the group consisting of a strip, a plate or a flat glass.	Page 9, line 27 to page 10, line 4. Page 46, line 4- 30. Page 26, line 28-30. Page 27, lines 13-21. Page 11, lines 14-35.
73. A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:	Page 2, lines 17-34; page 9, lines 7-22.
(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,	Page 9, lines 27-29; Figs. 3B, 4A, 4B, 6A and 6B; page 27, line 27 to page 28, line 16.
(b) placing said support in a chamber and subjecting said surface to one step of said synthesis and	Page 9, line 33 to page 10, line 4. Page 24, line 13 to page 29, line 13.
(c) placing said support in another reaction chamber and subjected said surface to another step of said surface to another step of said synthesis wherein (a)-(c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said reaction chambers comprises an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed wherein said support is selected from the group consisting of a strip, a plate or a flat glass.	Page 9, line 27 to page 10, line 4. Page 46, line 4- 30. Page 26, line 28-30. Page 27, lines 13-21. Page 11, lines 14-35.

### 37 C.F.R. §§ 1.601(m) and 1.608(b)

37 C.F.R. § 1.601(m) provides that a senior party in an interference is the party with the earliest effective filing date as to the count.

As noted, Applicants' present disclosure is entitled to the benefit of a filing date of April 17, 1996, filing date of USSN 08/634,053. In comparison, the earliest possible effective filing

date to which the '348 patent could be accorded benefit appears to be June 29, 2001, i.e., the filing date of USSN 09/896,572. Therefore, Applicants have an effective filing date over 5 years prior to the earliest possible effective filing date of the '348 patent.

In accordance with the provisions of 37 C.F.R. § 1.601(m), Applicants should be designated the Senior Party in the requested interference.

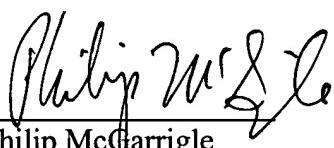
In view of Applicants' earlier effective filing date with respect to the '348 patent, no showing under 37 C.F.R. §1.608(b) is required.

**37 C.F.R. §1.607(b) - Request to Proceed with Special Dispatch**

In accordance with 37 C.F.R. §1.607(b), Applicants request that the Examiner proceed with special dispatch in declaring the requested interference.

Respectfully submitted,  
AFFYMETRIX, INC.

Date: 3-26-04

By:   
Philip McGarrigle  
Reg. # 31,395

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NOTICE OF ALLOWANCE AND FEE(S) DUE

7550 03/07/2003

AGILENT TECHNOLOGIES, INC.  
Legal Department, DL-129  
Intellectual Property Administration  
P O Box 7599  
Loveland, CO 80537-0599

EXAMINER  
FORMAN BETTY J  
ART UNIT CLASS-SUBCLASS  
1634 433-095000

DATE MAILED: 03/07/2003

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,572	06/29/2001	Jay K. Osas	10004187-1	7940

TITLE OF INVENTION: METHODS FOR MANUFACTURING ARRAYS

APPLN TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1300	\$300	\$1600	06/09/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-8SB (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I Review the SMALL ENTITY status shown above

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:  
A If the status is the same, pay the TOTAL FEE(S) DUE shown above

B If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A Pay TOTAL FEE(S) DUE shown above, or

B If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above

Applicant claims SMALL ENTITY status  
Sec. 37 CFR 1.27

II PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid Part B - Fee(s) Transmittal should be completed and returned if you are charging the fee(s) to your deposit account. section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted

III All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due

Page 1 of 4

PTOL-85 (REV 04-02) Approved for use through 01/31/2004

**EXHIBIT 2**  
**Request for Declaration of Interference**  
**USSN 10/722,032**

**PART B - FEE(S) TRANSMITTAL**

Complete and send this form, together with applicable fee(s), to: Mail Box ISSUE FEE  
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 Washington, D C 20231  
 Encl (703)746-4000

**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notifications of maintenance fees will be mailed to the first correspondence address as indicated unless corrected below or directed otherwise in Block 1; by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

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7550 03/07/2001  
**AGILENT TECHNOLOGIES, INC**  
 Legal Department, DL429  
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 Loveland, CO 80537-0599

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Certificate of Mailing or Transmission  
 I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above or being facsimile transmitted to the USPTO on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/350,572	06/29/2001	Jay K. Bass	10004187-1	7940

TITLE OF INVENTION: METHODS FOR MANUFACTURING AIRWAYS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1300	\$300	\$1600	06/09/2001

EXAMINER	ART UNIT	CLASS-SUBCLASS
FORMAN, BETTY J	1634	433-006000

I. Change of correspondence address or indication of "Fee Address" (37 CFR 1.36)

Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached

"Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 02-02, or more recent) attached Use of a Customer Number is required.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1. \_\_\_\_\_  
 2. \_\_\_\_\_  
 3. \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type):

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.  
 (A) NAME OF ASSIGNEE \_\_\_\_\_  
 (B) RESIDENCE: (CITY AND STATE OR COUNTRY) \_\_\_\_\_

Please check the appropriate assignee category or categories (will not be printed on the patent)       individual     corporation or other private group entity     government

4a. The following fee(s) are enclosed:

4b. Payment of Fee(s):

Issue Fee

A check in the amount of the fee(s) is enclosed

Publication Fee

Payment by credit card Form PTO-2038 is attached

Advance Order - # of Copies \_\_\_\_\_

The Commissioner is hereby authorized to charge the required fee(s), or credit any overpayment to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

Commissioner for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above

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(Date)

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This collection of information is required by 37 CFR 1.331. The information is required to obtain or retain a benefit by the public which is in file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 123 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete. Using existing, preparing, and maintaining the completed application form in the USPTO. The burden may vary depending on the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington DC 20231.

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PTO-15 (REV 04-02) Approved for use through 01/31/2004 OMB 0651-0033

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE



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United States Patent and Trademark Office  
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,572	05/29/2001	Jay K. Bass	10004187.1	7940
7350	03/07/2003			
AGILENT TECHNOLOGIES, INC. Legal Department, DL-429 Intellectual Property Administration P O. Box 7599 Loveland, CO 80537-0599			EXAMINER	
			FORMAN BETTY J	
			ART UNIT	PAPER NUMBER
			1624	
DATE MAILED: 03/07/2003				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)  
(application filed on or after May 29, 2000)

The patent term adjustment to date is 0 days. If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the term adjustment will be 0 days.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (<http://pair.uspto.gov>)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/196,372	06/19/2001	Jay K. Doss	10004187-1	7940
7190	01/07/2003			EXAMINER
AGILENT TECHNOLOGIES, INC				FORMAN BETTY J
Legal Department, DL-129				
Intellectual Property Administration				
P O Box 7599				
Loveland, CO 80537-0599				
UNITED STATES				
			ART UNIT	PAPER NUMBER
			1634	
			DATE MAILED: 03/07/2003	

## Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003; Final Rule, 67 Fed Reg 70847, 70849 (November 27, 2002)

The current fee schedule is accessible from: <http://www.uspto.gov/main/howtofees.htm>.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

<b>Notice of Allowability</b>	Application No	Applicant(s)	
	09/898,572	BASS ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

*- The MAILING DATE of this communication appears on the cover sheet with the correspondence address-*  
 All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTO-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1  This communication is responsive to Amendment A, filed 4 December 2002 and Examiner's amendments  
 2  The allowed claim(s) is/are 1-29  
 3  The drawings filed on 16 January 2002 are accepted by the Examiner  
 4  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (i)  
   a)  All   b)  Some\*   c)  None of the:  
     1  Certified copies of the priority documents have been received  
     2  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_  
     3  Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(e))  
   \* Certified copies not received: \_\_\_\_\_  
 5  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application)  
   (a)  The translation of the foreign language provisional application has been received  
 6  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

7.  A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient

8.  CORRECTED DRAWINGS must be submitted  
   (a)  Including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached  
     1  hereto or 2  to Paper No. \_\_\_\_\_  
   (b)  Including changes required by the proposed drawing correction filed \_\_\_\_\_ which has been approved by the Examiner  
   (c)  Including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. \_\_\_\_\_  
 Identifying indicia such as the application number (see 37 CFR 1.04(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9.  DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL

**Attachment(s)**

1  Notice of References Cited (PTO-892)  
 3  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 5  Information Disclosure Statements (PTO-1449), Paper No. \_\_\_\_\_  
 7  Examiner's Comment Regarding Requirement for Deposit of Biological Material  
 2  Notice of Informal Patent Application (PTO-152)  
 4  Interview Summary (PTO-413), Paper No. 9, 11, 13, 14  
 6  Examiner's Amendment/Comment  
 8  Examiner's Statement of Reasons for Allowance  
 9  Other

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Art Unit: 1634

Page 2

**Notice of Allowance**

1 This action is in response to amendments filed 4 December 2002 and further amendments discussed during interviews between the Examiner and Mr Stewart and Mr Leitereg during the period of January 29-31. The previous rejections in the Office Action of Paper No. 7 dated 5 September 2002 are withdrawn in view of the amendments. Further amendments to the claims suggested by the examiner and approved by Mr Leitereg are detailed below. The additional amendments place the claims in condition for allowance.  
Claims 1-29 are in condition for allowance.

**EXAMINER'S AMENDMENT**

2 An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Renumber Claims 19, 20 and 21 as Claims 21, 19 and 20 respectively (37 C F R 1.126 and MPEP 608.01 (j) and 608.01 (n) IV)

3 Authorization for this examiner's amendment was given in a telephone interview with Mr. Theodore Leiterer on 30 January 2003 and 31 January 2003

The application has been amended as follows:

- a In Claim 1, step (b), replace "placing" with - mounting---
- b In Claim 1, step (b), replace "into" with - in --
- c In Claim 1, step (c), replace "placing" with - mounting---
- d In Claim 1, step (c), replace "into" with - in --
- e In Claim 1, in the last line of the claim, replace "placed" with - mounted --
- f In Claim 1, before the period add, -- wherein said support is selected from the group consisting of a strip, a plate or a flat glass ---
- g In Claim 2, line 1, replace "placing" with - mounting --
- h In Claim 3, line 2, replace "placing" with - mounting --

#### **REASONS FOR ALLOWANCE**

4 The following is an examiner's statement of reasons for allowance:

The claims are drawn to a method for synthesizing an array of chemical compounds and/or biopolymers. The method comprises mounting a support in a flow cell and subjecting the support surface to one step of synthesis, mounting the support in another flow cell and subjecting the support surface to another step of synthesis and repeating the above steps to synthesize the array wherein the support is either a strip, a plate or a flat glass and wherein the flow cell comprises a housing with a chamber and an inlet and an outlet. In another embodiment the claims are drawn to a first step of depositing droplets of monomer addition reagents onto the surface of the support.

Kedar (U S Patent No 6,165,778, issued 26 December 2000) teaches a method of synthesis comprising moving a plurality of beads in suspension into and out of reaction chambers for sequential addition of monomers onto the beads to thereby synthesize polymers on the beads (Abstract). Kedar specifically teaches the method is drawn to synthesis on beads in suspension. However, Kedar does not teach or suggest the suspended support comprises a strip, plate or flat glass nor does Kedar teach that the suspended supports are mounted in the reaction chamber as instantly claimed. As such, the prior art of record does not teach or suggest the instantly claimed invention.

5 Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

#### Conclusion

6 Claims 1-29 are allowed.

7 Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196

✓  
BJ Forman, Ph D  
Patent Examiner  
Art Unit: 1634  
January 31, 2003

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THEODORE J. LEITERER

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being transmitted by facsimile to the U.S. Patent and Trademark Office on December 4, 2002, to facsimile number 703-872-9306, the Official Facsimile Number designated for Before Final responses to Technology Center TC 1600 (in Notice signed by Nicholas P. Gadic on 11/01/2001).

Signature Theodore J. Leiterer Date 12/4/02  
Name Theodore J. Leiterer

PATENTS  
Attorney Docket No. 10004187-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application: 09/896,572

Inventors: Jay K. Bass, et al.

Group Art Unit: 1634

Filed: June 29, 2001

Examiner: B. J. Forman

Title: METHODS FOR MANUFACTURING ARRAYS

Box Non-fee Amendment  
Assistant Commissioner for Patents  
Washington, D C 20231

Sir:

Amendment under 37 C.F.R. §1.111 and §1.115

This is responsive to the Office Action dated September 5, 2002, from the U.S. Patent and Trademark Office in the above-identified patent application. Please amend the above-identified application as follows

In the Claims

Please amend the claims as follows:

1 (amended) A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:

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**EXHIBIT 1**  
Request for Declaration of Interference  
USSN 10/722,032

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(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds.

(b) placing <sup>mounting</sup> said support <sup>in</sup> a chamber of a flow cell and subjecting said surface to one step of said synthesis and

(c) placing <sup>mounting</sup> said support <sup>in</sup> a chamber of another flow cell and subjecting said surface to another step of said synthesis

wherein (a) – (c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is <sup>mounted</sup> wherein said support is selected from the group consisting of a strip, a plate or a flat glass

2 (amended) A method according to Claim 1 further comprising placing said support after step (c) of said synthesis into a chamber of another flow cell and subjecting said surface to another step of said synthesis

3 (amended) A method according to Claim 1 wherein said preparing of said surface for the next step of said contacting comprises "n" number of steps and said method comprises independently placing a support into a chamber of one of "n" number of flow cells and subjecting said surface to a different step of said synthesis in each of said flow cells

4 (amended) A method according to Claim 1 wherein reagents for step (a) of said synthesis are in fluid communication with said flow cell of step (a) and reagents for step (b) of said synthesis are in fluid communication with said flow cell of step (b) and wherein the fluid communication of the flow cell of step (a) is separate from the fluid communication of the flow cell of step (b).

5. (amended) A method according to Claim 1 wherein at least one of said steps of said synthesis comprises washing said surface.

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13. (amended) A method for synthesizing an array of biopolymers on the surface of a support wherein said synthesis comprises a plurality of monomer additions, said method comprising:

(a) depositing droplets of monomer addition reagents on a surface of said support,

(b) placing said support into a chamber of a flow cell and subjecting said surface to a step of said synthesis that is subsequent to a monomer addition and

(c) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis that is subsequent to step (b) wherein said steps are repeated until said array of biopolymers is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed and wherein said flow cell of (b) is dedicated to said step (b) and said flow cell of (c) is dedicated to step (c)

14. (amended) A method according to Claim 13 wherein each of said steps (a) and (b) comprises a wash.

16. (amended) A method according to Claim 13 wherein step (b) comprises subjecting said surface to an oxidizing agent

17. (amended) A method according to Claim 13 wherein step (c) comprises subjecting said surface to an agent for removing a protecting group.

22. (amended) A method according to Claim 19 wherein said fluid is an organic solvent

27. (amended) A method according to claim 26 comprising forwarding data comprising a result obtained from a reading of the array.

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29 (amended) A method according to claim 26 comprising receiving data comprising a result of an interrogation obtained by the reading of the array.

Claims 30-49 were withdrawn from consideration in the aforementioned Office Action. Please cancel Claims 30-49 without prejudice to Applicant's filing of one or more divisional applications to the subject matter of Claims 30-49.

#### REMARKS

Applicants request reconsideration of their application in view of the foregoing amendments and the discussion that follows. The status of the claims as of this response is as follows: Claims 1-29 are pending in the above-mentioned patent application. Claims 30-49 were withdrawn from consideration in the aforementioned Office Action and have been canceled herein without prejudice to Applicant's filing of one or more divisional applications to the subject matter of claims 30-49. Claims 1, 2-5, 13, 14, 16, 17, 22, 27 and 29 have been amended herein.

Attached hereto is a marked-up version of the changes made to the specification and the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE." Although not required, also attached hereto is a "CLEAN COPY OF CURRENT VERSION OF PENDING CLAIMS."

#### The Amendment

Claim 1 was amended to recite that the method comprises contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds. Claim 1 also recites that the steps (a) - (c) are repeated until said array of chemical compounds is synthesized on said surface. Support therefor is in the Specification, for example, page 7, lines 18-20, page 4, line 12, page 6, line 6, and page 14, lines 8-14. Claim 1 now recites that each of the flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed. Support therefor is in the Specification, for example, page 14, lines 20-29.

Claim 2 was amended to provide proper reference back to the base claim.

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Attorney Docket No 10004187-1

Claim 3 was amended to recite that the "n" number of steps includes (b) and (c). Support therefor is in the Specification, for example, original Claim 3 and page 4, lines 12-14.

Claim 4 was amended to recite that the fluid communication of the flow cell of step (b) is separate from the fluid communication of the flow cell of step (c). Support therefor is in the Specification, for example, original Claim 4.

Claim 5 was amended to recite that at least one of said steps of said synthesis comprises washing said surface.

Claim 13 was amended to recite that the method comprises depositing droplets of monomer addition reagents on a surface of the support and to recite that the steps (a) – (c) are repeated until the array of biopolymers is synthesized on the surface. Support therefor is in the Specification, for example, page 7, lines 18-20, page 4, line 12, page 5, line 6, and page 14, lines 8-14. Claim 13 was also amended to recite that each of the flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed. Support therefor is in the Specification, for example, page 14, lines 20-29. Claim 1 also recites that the flow cell of (b) is dedicated to step (b) and the flow cell of step (c) is dedicated to step (c). Support therefor is in the Specification, for example, page 14, lines 16-18.

Claim 14 was amended to refer to each of steps (a) and (b). Support therefor is in the Specification, for example, original Claim 14.

Claims 16 and 17 were amended to provide proper reference back to the base claim.

Claim 22 was amended to change its dependency to Claim 19.

Claim 27 was amended to recite comprising. Support therefor is in the Specification, for example, original Claim 27.

Claim 29 was amended to recite comprising. Support therefor is in the Specification, for example, original Claim 29.

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Attorney Docket No. 10004187-1

Information Disclosure Statement

Applicant acknowledges the Examiner's indication that the references on Applicant's PTO 1449 were reviewed and considered.

Rejection under 35 U.S.C. §112

Claims 1-29 were rejected under the second paragraph of the above code section as being Indefinite, asserts the Examiner, for failure to particularly point out and distinctly claim the subject matter that applicant regards as the Invention.

The Examiner contends that Claims 1-12 are Indefinite in Claim 1 because the claim is drawn to a method for synthesizing an array of chemical compounds but the claim does not recite method steps of array synthesis or chemical compounds. Claim 1 was amended to recite positive and active method steps for synthesizing an array of chemical compounds, thus obviating this particular ground of rejection.

Applicant submits that the above amendment to Claim 3 obviates the rejection of Claim 3 under the above code section.

Applicant believes that the amendment to Claim 4 obviates the rejection of Claim 4 under the above code section.

The Examiner contends that Claims 13-29 are indefinite in Claim 13 because the claim is drawn to a method for synthesizing an array of biopolymers but the claim does not recite method steps of array synthesis or biopolymers. Applicant submits that the amendments to Claim 13 reciting positive and active method steps obviate this ground of rejection.

Claim 22 was amended to provide proper antecedent basis, thereby obviating the rejection of Claim 22 under the above code section.

The rejection of Claims 26-29 is overcome by the amendments to Claim 13, which clearly recite that the method steps are repeated until the array is formed. Thus, Claim 13 provides proper antecedent basis for Claims 26-29.

Applicant submits that the amendments to Claims 27 and 29 obviate the rejection of those claims under the above code section.

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THEODORE J LEITERER

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U S Serial No 09/896,572

Attorney Docket No 10004187-1

Rejection under 35 U.S.C. §102

Claims 1-9, 12-18, 21-23 and 25-26 were rejected under 35 U.S.C. 102(e) as being anticipated by Bass, et al (U.S. Patent No. 6,440,669 B1, filed 10 November 1999) (Bass).

Bass discloses methods, devices and apparatus for carrying out multiple chemical reactions such as *in situ* synthesis of polynucleotides on a surface comprising an array of discrete sites. Molecules are deposited at a predetermined number of discrete sites on the surface for reaction at the discrete sites. The surface is positioned relative to an outlet of a fluid ejection device, which is activated to dispense a small volume of a fluid through the outlet to the surface to provide uniform coating of a continuous region of the surface comprising a multiple of the discrete sites. The fluid is dispensed as uniform particles having a diameter such that the uniform particles form a sheet to coat the continuous region of the surface.

The Examiner asserts that Bass discloses a method for synthesizing an array of chemical compounds wherein at least two of the steps are carried out by placing a support having a surface into a chamber of a flow cell and subjecting the surface to one step of the synthesis and placing the support into a chamber of another flow cell and subjecting the surface to another step of the synthesis. The Examiner cites column 16, lines 7-63, in support of the above assertion.

Applicant respectfully traverses the above ground of rejection. In the disclosure at the cited text, Bass merely moves a support from one linear stage to another linear stage within the apparatus. The linear stages are supported by respective platforms. The Examiner has not pointed to any disclosure of flow cells. At the text referred to by the Examiner, phosphoramidite reagents are deposited at linear stage 39 of platform 32. The substrate wafer 36 is then moved to linear stage 41 of platform 33, where an ultrasonic fluid ejection device is activated to dispense a liquid reagent that comprises an oxidizing reagent to uniformly coat the surface (column 16, lines 14-20). Bass indicates that additional steps in the synthesis of an array are carried out at platform 33 of apparatus 30. Ultrasonic fluid ejection is employed to dispense a wash liquid, a deblocking reagent (column 16, lines 43-46), and a wash liquid (column 16, lines 33-35).

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As mentioned above, the Examiner has not pointed to any disclosure in Bass indicating the Bass uses flow cells as part of his method. At column 7, lines 19-22, Bass distinguishes his invention from the use of flow cells. Bass indicates that his method produces a thinner layer of liquid deposited on a surface than that produced by prior methods such as flow cell assembly.

Another point to be mentioned is that Bass performs multiple steps at one linear stage. On the other hand, in the present invention, the step (b) is carried out in a different flow cell than step (c).

With regard to the Examiner's rejection of Claims 2-12, which depend from Claim 1, the same confusion appears to exist between the linear stages and platforms of Bass and the flow cells of the present invention. The disclosure of Bass relates to linear stages and not to flow cells. As mentioned above, Bass distinguishes his method from that of flow cell assembly.

The aforementioned arguments apply with equal weight to the rejection of Claims 13-18, 21-23 and 25-26.

Claims 1-9, 13, 14, 16-18, 21-23 and 25-26 were rejected under 35 U.S.C. 102(b) as being anticipated by Ellman (U.S. Patent No. 5,288,514, issued 22 February 1994) (Ellman)

Ellman discloses methods, compositions and devices for synthesis of therapeutically useful compounds. Without in any way acquiescing in the argument of the Examiner with respect to the relevance of Ellman's disclosure of pins and containers for reagents, Applicant submits that the claims as amended obviate this ground of rejection. The claims now recite that the flow cells comprise a housing with a chamber and a fluid inlet and a fluid outlet for flowing fluids into and through the chamber in which the support is placed.

#### Rejection under 35 U.S.C. §103

Claims 1-9, 12-18, 21-23 and 25 were rejected under 35 U.S.C. 103(a) as obvious over Blanchard WO/98/41531, published 24 September 1998) (Blanchard). Blanchard discloses a method of oligonucleotide synthesis consisting of coupling a first nucleotide to a second nucleotide in a high surface tension solvent. Blanchard also



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discloses microdroplets of a solution comprising a solvent having a specified boiling point. The microdroplets may be employed for the synthesis of chemical species such as biopolymers.

The Examiner contends that Blanchard teaches a method for synthesizing an array of chemical compounds on the surface of a support wherein the synthesis comprises a plurality of steps. The Examiner asserts that Blanchard's method comprises at least two of the steps being performed by placing a support having a surface into a chamber of a flow cell and subjecting the surface to one step of the synthesis and placing the support into a chamber of another flow cell and subjecting the surface to another step of synthesis.

Applicant submits that Blanchard makes no disclosure or suggestion of employing flow cells in the manner employed in Applicant's invention. Blanchard discloses nothing more than the known technique of using one flow cell to carry out multiple processing steps. At page 58, lines 1-12, Blanchard indicates that after a print head cycle, the substrate is moved from the print head assembly to flow cell 30, which treats the substrate by exposing it to selective fluids in order to rinse off unconnected monomers, oxidize and deprotect the substrate. Once rinsed, the substrate is moved again to the printing head assembly for a further cycle of monomer deposits.

The Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the apparatus comprising multiple flow cells of Blanchard to his method comprising multiple treatment steps wherein numerous different reagent solutions are supplied to a support within a flow cell. The Examiner asserts that Blanchard, by applying his multiple flow cell apparatus to his multiple reagent-treatment steps and moving the support to and from flow cells, each specific for a different reagent solution, one would eliminate the need to remove a first reagent solution before adding a second reagent solution and the need to remove second reagent solution before adding a third and etc. Additionally, continues the Examiner, one would eliminate the possibility of contamination between the different reagent solutions within the flow cell. Therefore, concludes the Examiner, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was

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made to apply the multiple flow cell apparatus of Blanchard to his method comprising multiple flow cell-treatment steps for the obvious benefits

Applicant submits that the above argument and conclusion is contrary to the teachings of the reference and is the result of hindsight reconstruction of the prior art based on Applicant's disclosure. Blanchard (page 58, lines 1-12) states that, after a print head cycle, treating transport 23 is used to move the substrate from the print head assembly to flow cell 30, which "treats" the substrate by exposing it to selective fluids in order to rinse off unconnected monomers, oxidize, and deprotect the substrate. Once rinsed, the substrate is moved again to print head assembly 24 for a further cycle of monomer deposits and then rinsed again in the flow cell. The steps are repeated numerous times to build desired biopolymer sequences. Accordingly, Blanchard discloses nothing more than conducting the processing steps in one flow cell.

In the paragraph bridging pages 74 and 75, Blanchard discloses an automated synthesis system where there are multiple flow cells. It is clear from this disclosure that each flow cell is employed to conduct multiple processing steps consistent with the teaching at page 58 above. At the top of page 75, Blanchard states that each flow cell is checked to see whether it is done with treating the wafer. If the treatment is done, the wafer is transferred to scanning arm 44. Applicant submits that, if each flow cell did not perform multiple processing steps, then the wafer would not be transferred to the scanning arm. Rather, Fig. 14 of Blanchard would show one wafer moving between several flow cells before moving to the scanning arm. Otherwise, the substrate would not be fully processed before the next monomer deposit is made. Blanchard's disclosure of a system with multiple flow cells relates only to multi-tasking, that is, concomitantly synthesizing arrays on the surface of several substrates. Blanchard makes no disclosure or suggestion to modify the teaching of the reference in the manner in which the Examiner has done.

The Federal Circuit has held that the mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification (*In re Fine*, 837 F.2d 1071, 5 USPQ 2d 1596 (Fed. Cir. 1988)). In the present situation there is no teaching or suggestion in Blanchard to use a single flow cell for anything other than conducting

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several processing steps such as rinsing, oxidizing and deprotecting. It is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Frisch*, 972 F. 2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992), quoting *In re Fine*, *supra*.

For the reasons given above, the Examiner has not established a *prima facie* case of obviousness. Accordingly, the burden is not on Applicant to show that the claimed placing the support into "another" flow cell is either different or non-obvious over that of Blanchard.

The aforementioned arguments apply equally to the rejection of Claims 1-9, 12-18, 21-23 and 25.

Claims 10 and 11 were rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard as applied to Claim 1 above and further in view of Tavlarides, et al. (U.S. Patent No. 4,284,800, issued 13 October 1981) (Tavlarides). Tavlarides discloses a liquid-liquid jet contactor process and apparatus in which a jet of fluid is arranged to flow through a coaxial, co-currently flowing stream of a second fluid, both of which fluids are immiscible or partially miscible, and, preferably, one or both of the fluids are continuously recycled.

The Examiner argues that Blanchard teaches a method for synthesizing an array of biopolymers on the surface of a support wherein the synthesis comprise a plurality of monomer additions, the method comprising: placing a support into a chamber of a flow cell and subjecting the surface to a step of synthesis subsequent to monomer addition and placing the support into a chamber of another flow cell and subjecting the surface to another subsequent step of synthesis. The Examiner recognizes that Blanchard is silent regarding determining a condition of or purification of the fluid exiting the outlet. However, asserts the Examiner, exit fluid analysis was well known in the art at the time the claimed invention was made as taught by Tavlarides, who specifically teach analysis of the exit fluid permits recycling of the fluid and provide information regarding a reaction that has occurred within the flow cell (column 5, lines 17-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made, concludes the Examiner, to apply the exit fluid analysis of Tavlarides to the fluid exiting the flow cells of Blanchard to thereby analyze flow cell reactions and recycle

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reagent fluids as taught by Tavlarides. The Examiner asserts that one skilled in the art would have been motivated to analyze flow cell reaction to thereby maintain quality control of flow cell reactions. One skilled in the art would also have been motivated to recycle reaction fluids for the obvious benefits of economy of reagents.

Blanchard is deficient in teaching or rendering obvious Applicant's invention as explained above. Accordingly, Claims 10 and 11 are not obvious in view of Blanchard and Tavlarides. Furthermore, contrary to the assertion of the Examiner, Tavlarides does not specifically teach that analysis of the exit fluid permits recycling of the fluid and provides information regarding a reaction that has occurred within a flow cell. The teaching of Tavlarides is directed to a specific recycling format. As indicated above, Tavlarides discloses a liquid-liquid jet contactor process and apparatus in which a jet of fluid is arranged to flow through a coaxial, co-currently flowing stream of a second fluid, both of which fluids are immiscible or partially miscible, and, preferably, one or both of the fluids are continuously recycled. There is no teaching in Tavlarides relating to flow cells as defined in the present claims or as mentioned in Blanchard. Tavlarides is concerned with improvements in the liquid jet technique for contacting two liquids.

As mentioned above, it is impermissible to use the claimed invention as an instruction manual or template to piece together the teachings of the prior art so that the claimed invention is rendered obvious. *In re Frisch*, 972 F. 2d 1260, 23 USPQ 2d 1780 (Fed. Cir. 1992), quoting *In re Fine*, *supra*. One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. *In re Frisch*, *supra*. Tavlarides concerns are distinct from that of Blanchard and that of the present invention. At column 2, lines 58-63, Tavlarides discusses one of the disadvantages of the prior art technique that is overcome with his invention. Tavlarides states that the small change in chemical composition usually occurring for short contact times may present a serious obstacle to accurate measurement of transfer to or from a fluid making a single pass through the reactor. Tavlarides indicates that recycling of fluid allows significantly greater amounts to accumulate. Thus, it is readily seen that Tavlarides disclosure is not relevant to the instant claims.

Claims 19 and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard as applied to Claim 13 above and further in view of Tavlarides. For the

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reasons given above with respect to the rejection of Claims 10 and 11, the combination of Blanchard and Tavlarides does not render obvious the invention of Claims 19 and 20.

Claim 24 was rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard in view of Heyneker (U.S. Patent No. 6,057,100, issued 2 May 2000) (Heyneker). Without acquiescing in the position of the Examiner, Applicant submits that Blanchard is deficient as explained above and that Heyneker does not cure the deficiencies of Blanchard. Accordingly, Claim 24, being dependent on Claim 13, is patentable over the combination of the references.

Claims 26-29 were rejected under 35 U.S.C. 103(a) as being unpatentable over Blanchard in view of Abraham-Fuchs, *et al* (U.S. Patent Application No. 2002/0111741 A1, filed 15 February 2001) (Abraham-Fuchs). Without acquiescing in the position of the Examiner, Applicant submits that Blanchard is deficient as explained above and that Abraham-Fuchs does not cure the deficiencies of Blanchard. Accordingly, Claims 26-29, being dependent on Claim 13, are patentable over the combination of the references.

#### Obviousness-type Double Patenting

Claims 1-25 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,440,669 B1 (Bass). The Examiner contends that, although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claim are drawn to a method of making an array and differ only in the patent methods are drawn to a species of array and the instant claims are drawn to a genus.

As indicated in M.P.E.P. section 804, a double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103 except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

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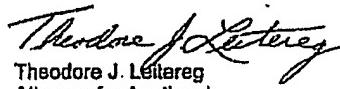
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Applicant respectfully traverses the above ground of rejection. As explained above, the Examiner has not pointed to any disclosure in Bass regarding the use of flow cells. Claims 1-18 of Bass do not refer to flow cells. Bass merely moves a support from one linear stage to another linear stage within his apparatus. Claims 1-18 of Bass are directed to dispensing a volume of liquid to uniformly coat the entire surface having the discrete sites. As mentioned above, at column 7, lines 19-22, Bass distinguishes his invention from the use of flow cells. Bass indicates that his method produces a thinner layer of liquid deposited on a surface than that produced by prior methods such as flow cell assembly. It is clear from the above that there is no genus-species relationship between dispensing a volume of liquid to uniformly coat the entire surface having the discrete sites of Claims 1-18 of Bass and the flow cells of the present claims. Bass neither discloses nor suggests the present invention and the present claims are not suggested by Claims 1-18 of Bass. Accordingly, Claims 1-18 of Bass do not render obvious Claims 1-25 of the present invention. No terminal disclaimer is necessary.

CONCLUSION

Claims 1-29 satisfy the requirements of 35 U.S.C. §112, 102 and 103 and do not circumscribe the judicially created doctrine of obviousness-type double patenting. Allowance of the above-identified patent application, it is submitted, is in order.

Respectfully submitted,

  
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VERSION WITH MARKINGS TO SHOW CHANGES MADEIn the Claims

The claims have been amended as follows:

1. (amended) A method for synthesizing an array of chemical compounds on the surface of a support [wherein said synthesis comprises a plurality of steps], said method comprising [performing at least two of said steps by]:

(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds.

(b[a]) placing said [a] support [having a functionalized surface] into a chamber of a flow cell and subjecting said surface to one step of said synthesis and

(c[b]) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis

wherein (a) – (c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed.

2. (amended) A method according to Claim 1 further comprising placing said support after step (c[b]) of said synthesis into a chamber of another flow cell and subjecting said surface to another step of said synthesis.

3 (amended) A method according to Claim 1 wherein said synthesis comprises "n" number of steps including (b) and (c) and said method comprises independently placing a support into a chamber of one of "n" number of flow cells and subjecting said surface to a different step of said synthesis in each of said flow cells

4 (amended) A method according to Claim 1 wherein reagents for step (b[a]) of said synthesis are in [separate] fluid communication with said flow cell of step (b[a]) and reagents for step (c[b]) of said synthesis are in [separate] fluid communication with said



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flow cell of step (c[b]) and wherein the fluid communication of the flow cell of step (b) is separate from the fluid communication of the flow cell of step (c).

5 (amended) A method according to Claim 1 wherein at least one of said steps of said synthesis comprises [contacting said surface with a fluid reagent and] washing said surface.

13 (amended) A method for synthesizing an array of biopolymers on the surface of a support wherein said synthesis comprises a plurality of monomer additions, said method comprising;

(a) depositing droplets of monomer addition reagents on a surface of said support, [after each of said monomer additions]

(b[a]) placing said support into a chamber of a flow cell and subjecting said surface to a step of said synthesis that is subsequent to a monomer addition and

(c[b]) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis that is subsequent to step (b[a]) wherein said steps are repeated until said array of biopolymers is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed and wherein said flow cell of (b) is dedicated to said step (b) and said flow cell of (c) is dedicated to step (c).

14 (amended) A method according to Claim 13 wherein one [each] of said steps (b) and (c) comprises a wash.

16. (amended) A method according to Claim 13 wherein step (b[a]) comprises subjecting said surface to an oxidizing agent.

17 (amended) A method according to Claim 13 wherein step (c[b]) comprises subjecting said surface to an agent for removing a protecting group.

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22. (amended) A method according to Claim 19 [18] wherein said fluid is an organic solvent

27 (amended) A method according to claim 26 comprising forwarding data comprising [representing] a result obtained from a reading of the array

29 (amended) A method according to claim 26 comprising receiving data comprising [representing] a result of an interrogation obtained by the reading of the array.

Claims 30-49 have been canceled without prejudice to Applicant's filing of divisional applications to the subject matter of these canceled claims

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CLEAN COPY OF CURRENT VERSION OF PENDING CLAIMS

1. (amended) A method for synthesizing an array of chemical compounds on the surface of a support, said method comprising:

(a) contacting a surface of said support with a fluid reagent for synthesizing said chemical compounds,

(b) placing said support into a chamber of a flow cell and subjecting said surface to one step of said synthesis and

(c) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis

wherein (a) – (c) are repeated until said array of chemical compounds is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed.

2. (amended) A method according to Claim 1 further comprising placing said support after step (c) of said synthesis into a chamber of another flow cell and subjecting said surface to another step of said synthesis

3. (amended) A method according to Claim 1 wherein said preparing of said surface for the next step of said contacting comprises "n" number of steps and said method comprises independently placing a support into a chamber of one of "n" number of flow cells and subjecting said surface to a different step of said synthesis in each of said flow cells.

4. (amended) A method according to Claim 1 wherein reagents for step (a) of said synthesis are in fluid communication with said flow cell of step (a) and reagents for step (b) of said synthesis are in fluid communication with said flow cell of step (b) and wherein the fluid communication of the flow cell of step (a) is separate from the fluid communication of the flow cell of step (b).

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5. (amended) A method according to Claim 1 wherein at least one of said steps of said synthesis comprises washing said surface.

6. A method according to Claim 1 wherein said chemical compounds are polymers

7. A method according to Claim 6 wherein said polymers are biopolymers.

8. A method according to Claim 1 wherein said flow cells comprise a holder for said support

9. A method according to Claim 1 wherein said flow cells comprise at least one inlet and an outlet.

10. A method according to Claim 9 wherein a condition of fluid exiting said outlet is determined and based on said determination at least a portion of said fluid is directed to said inlet or to a waste container for said fluid

11. A method according to Claim 9 wherein fluid exiting said outlet is subjected to purification and a condition of said fluid is determined and based on said determination at least a portion of said fluid is directed to said inlet or to a waste container for said fluid

12. A method according to Claim 9 wherein a wash solution and a reagent for said synthesis are independently directed to said inlet.

13. (amended) A method for synthesizing an array of biopolymers on the surface of a support wherein said synthesis comprises a plurality of monomer additions, said method comprising:

(a) depositing droplets of monomer addition reagents on a surface of said support,

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(b) placing said support into a chamber of a flow cell and subjecting said surface to a step of said synthesis that is subsequent to a monomer addition and

(c) placing said support into a chamber of another flow cell and subjecting said surface to another step of said synthesis that is subsequent to step (b) wherein said steps are repeated until said array of biopolymers is synthesized on said surface and wherein each of said flow cells comprises a housing with a chamber and an inlet and an outlet for introduction and removal of fluids in the chamber in which the support is placed and wherein said flow cell of (b) is dedicated to said step (b) and said flow cell of (c) is dedicated to step (c).

14. (amended) A method according to Claim 13 wherein each of said steps (a) and (b) comprises a wash.

15. A method according to Claim 13 wherein said biopolymers are polynucleotides

16 (amended) A method according to Claim 13 wherein step (b) comprises subjecting said surface to an oxidizing agent.

17 (amended) A method according to Claim 13 wherein step (c) comprises subjecting said surface to an agent for removing a protecting group

18. A method according to Claim 13 wherein said flow cells comprise at least one inlet and an outlet and a holder for said support.

19 A method according to Claim 13 wherein a condition of fluid exiting said flow cell is determined and based on said determination at least a portion of said fluid is directed to said flow cell or to a waste container for said fluid

20 A method according to Claim 18 wherein fluid exiting said flow cell is subjected to purification and a condition of said fluid is determined and based on said

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determination at least a portion of said fluid is directed to said flow cell or to a waste container for said fluid.

21 A method according to Claim 18 wherein a wash solution and a reagent for said synthesis are independently directed to said inlet.

22. (amended) A method according to Claim 19 wherein said fluid is an organic solvent.

23. A method according to Claim 13 wherein said biopolymers are peptides.

24 A method according to Claim 13 wherein said biopolymers are synthesized on said surface in multiple arrays and said support is subsequently diced into individual arrays of biopolymers on a support.

25. A method according to Claim 13 wherein reagents for said first step of said synthesis are in separate fluid communication with said first flow cell and reagents for said second step of said synthesis are in separate fluid communication with said second flow cell.

26. A method according to claim 13 further comprising exposing the array to a sample and reading the array.

27. (amended) A method according to claim 26 comprising forwarding data comprising a result obtained from a reading of the array

28. A method according to claim 27 wherein the data is transmitted to a remote location

29. (amended) A method according to claim 26 comprising receiving data comprising a result of an interrogation obtained by the reading of the array

**INTERFERENCE INITIAL MEMORANDUM**

To the Board of Patent Appeals and Interferences:

An interference is proposed involving the following 2 parties

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Junior Party Bass et al.	09/896,572	— 06/29/2001	6,649,348	11/18/2003

If the involved is a patent, have its maintenance fees been paid? Yes        No        Not due yet X

Proposed priority benefit (list all intervening applications necessary for continuity):

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
None	None	None	None	None
The claim(s) of this party corresponding to this count:				
PATENTED OR PATENTABLE PENDING CLAIMS			UNPATENTABLE PENDING CLAIMS	
Patented claims 1-29			N/A	
The claim(s) of this party NOT corresponding to this count:				
PATENTED OR PATENTABLE PENDING CLAIMS			UNPATENTABLE PENDING CLAIMS	
None			N/A	

PARTY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
Senior Party Goldberg et al.	10/722,032	11/25/2003	N/A	N/A

If the involved is a patent, have its maintenance fees been paid? Yes        No        Not due yet N/A

Proposed priority benefit (list all intervening applications necessary for continuity):

COUNTRY	APPLICATION NO.	FILING DATE	PATENT NO., IF ANY	ISSUE DATE, IF ANY
USA	09/716,669	11/20/2000	N/A	N/A
USA	09/716,507	11/20/2000	N/A	N/A
USA	09/427,850	10/26/1999	6,239,273	5/29/01
USA	09/244,568	2/4/99	6,307,042	10/23/01
USA	09/093,843	5/22/98	N/A	N/A
WIPO	PCT/US97/06535	4/16/97	N/A	N/A
USA	08/634,053	4/17/96	5,959,098	9/28/99

The claim(s) of this party corresponding to this count:

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
Patentable pending claims 50-78	None

The claim(s) of this party NOT corresponding to this count:

PATENTED OR PATENTABLE PENDING CLAIMS	UNPATENTABLE PENDING CLAIMS
None	None

*(Check off each step, if applicable)* **INSTRUCTIONS**

- 1. Obtain all files listed above.
- 2. Confirm that the proposed involved claims are still active and all corrections and entered amendments have been considered. The patents must not be expired for, among other things, failure to pay a maintenance fee (Check PALM screen 2970).
- 3. If one of the involved files is a published application or a patent, check for compliance with 35 U.S.C. 135(b).
- 4. Obtain a certified copy of any foreign benefit documents where necessary (37 CFR 1.55(a)).
- 5. Discuss the proposed interference with an Interference Practice Specialist in your Technology Center.

DATE	PRIMARY EXAMINER (signature)	ART UNIT	TELEPHONE NUMBER
DATE	INTERFERENCE PRACTICE SPECIALIST or TECHNOLOGY CENTER DIRECTOR (signature)	TELEPHONE NUMBER	